

**PCT**INTERNATIONAL SEARCH REPORT  
(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 53436/145	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below
International application No. <b>PCT/CA2004/001974</b>	International filing date ( <i>day/month/year</i> ) 17 November 2004 (17-11-2004)	Priority date ( <i>day/month/year</i> ) 17 November 2003 (17-11-2003)
Applicant TM BIOSCIENCE CORPORATION ET AL		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
  - a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
  - b. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.
2. ☐ Certain claims were found unsearchable (see Box No. II).
3. ☐ Unity of invention is lacking (see Box No. III).
4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows :
5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. With regard to the **drawings**,
  - a. the figure of the **drawings** to be published with the abstract is Figure No. \_\_\_\_\_

☐ as suggested by the applicant.

☐ as selected by this authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.
  - b. ☒ none of the figures is to be published with the abstract.

**Box No. I** Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
  - a. type of material
    - ☒ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material
    - ☒ in written format
    - ☒ in computer readable form
  - c. time of filing/furnishing
    - ☒ contained in the international application as filed.
    - ☒ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statement that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments :

**A. CLASSIFICATION OF SUBJECT MATTER**IPC<sup>7</sup>: C12Q-1/68**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC<sup>7</sup>: C12, C07, A61

Documentation searched other than minimum documentation to the extent that such documents are included in the fields

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms)

Canadian Patent Database, DELPHION, USPTO, ESPACENET, PUBMED, GENBANK, GENESEQ

Multiplex, PCR, polymerase chain amplification, primer extension, thrombosis, single nucleotide polymorphism, point mutation, SNP, factor V Leiden, G1691, prothrombin, G20210A, factor II, C677T, methylenetetrahydrofolate reductase, MTHFR, A1298C, factor XIII, G4377T, tissue specific factor plasma inhibitor, TFPI, C536T, allele specific, and tagged

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant	Relevant to claim No(s).
Y	EP 1,398,388 A2 (CULLEN, P. et al.) 17 March 2004 Abstract; Example 1; Table 1	1-7, 9-12, 14 and 15
Y	ENDLER, G. et al. Multiplexed mutagenically separated PCR: simultaneous single-tube detection of the factor V R506Q (G1691A), the prothrombin G20210A, and the methylenetetrahydrofolate reductase A223V (C677T) variants. Clin. Chem. February 2001, Vol.47, No. 2, Pages 333-335 Pages 333-334, bridging paragraph; Figure 1	1-7, 9-12, 14 and 15

☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

## \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier application or patent but published on or after the international filing date
- "L" document which may throw doubt on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

10 March 2005 (10-03-2005)

Date of mailing of the international search report

29 April 2005 (29-04-2005)

Name and mailing address of the ISA/CA  
Canadian Intellectual Property Office  
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Gatineau, Quebec K1A 0C9

Facsimile No: 001(819)953-2476

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No(s).
Y	NEITZEL, B. et al. Easy, accurate and reliable screening for SNPs by ion pair/reverse phase HPLC: simultaneous detection of factor V G1691A, prothrombin G20210A and methylenetetrahydrofolate reductase C677T variants. Clin. Lab. July-August 2003, Vol. 49, Nos. 7-8, Pages 313-318 Abstract; Figure 1	1-7, 9-12, 14 and 15
Y	WO 00/47766 A1 (GIBSON, N. J. et al.) 17 August 2000 Abstract; page 2, line 9 to page 4, line 3	1-7, 9-12, 14 and 15
Y	WO 02/059355 A2 (KOBLE, D. et al.) 1 August 2002 Page 5, lines 8-15; Table I	1-7, 9-12, 14 and 15
A	GB2,338,062 A (BOWEN, D. et al.) 08 December 1999 Page 91, line 27	8, 13, 16 and 17
A	WO 2004/072887 A2 (ROBERTS, G. et al.) 26 August 2004 Page 56, SEQ ID NO 4	8, 13, 16 and 17
A	WO 00/11034 A1 (KLEESIEK, K. et al.) 2 March 2000 Page 4, line 16	8, 13, 16 and 17

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

International application No.  
PCT/CA2004/001974

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
EP1398388 A2	17-03-2004	DE10237073 A1	19-02-2004
WO0047766 A1	17-08-2000	AU2447100 A	29-08-2000
		EP1151136 A1	07-11-2001
		GB9902971D D0	31-03-1999
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		BR0206747 A	30-11-2004
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		WO02059354 A2	01-08-2002
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		AU5736899 A	14-03-2000
		CA2340460 A1	02-03-2000
		DE69918128D D1	22-07-2004
		EP1105423 A1	13-06-2001
		US6521410 B1	18-02-2003